

AMENDMENTS TO THE DRAWINGS

The attached sheets of drawings include changes to Figures 6, 13, 14A, and 14B to include appropriate sequence identifiers. *No new matter has been added.*

Attachment: Replacement sheet
 Annotated sheet showing changes

REMARKS

Claims 1-48 were pending in the application. Claims 22-48 have been canceled, without prejudice, as being drawn to a non-elected invention. Claims 1, 3, 4, 6, 8, 9, 10, 13, 15, and 17 have been amended. Accordingly, upon entry of the present amendment, claims 1-21 will remain pending in the application.

Support for the amendments to the claims and for the new claims may be found throughout the specification and claims as originally filed. Specifically, support for the amendments to claim 1 to recite “said 3’ recognition sequence also comprising a DNA modification enzyme recognition sequence” may be found at, for example, page 22, lines 4-15 of the specification; and support for the amendments to claims 9 and 10 to recite “a starting DNA construct” may be found at, for example, page 23, lines 8-19 of the specification. *No new matter has been added.*

Any amendments to and/or cancellation of the claims are not to be construed as an acquiescence to any of the rejections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the subject matter of the claims as originally filed in this or a separate application(s).

Election/Restriction

Group I (claims 1-21) directed to a method of assembling several DNA units in sequence and *species* (1) directed to one or more of the DNA units being derived from polyketide synthesizing enzyme domain DNA sequences (claim 17) were elected by Applicants with traverse. Applicants acknowledge the Examiner’s indication that the restriction requirement has been deemed to be proper and has, therefore, been made final. Accordingly, claims 22-48 have been canceled as being directed to a non-elected invention.

It is Applicants’ understanding that upon allowance of a generic claim, they will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141 *et seq.*

Sequence Rules Compliance

The Examiner is of the opinion that

[t]his application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). For example, see pages 26-28 and 40 of the specification. However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicants have amended the specification and Figures to add sequence identifiers where appropriate including the specific sections noted by the Examiner. Additionally, the specification has been amended to incorporate a sequence listing that includes the sequences noted by the Examiner at paragraph 2 of the Office Action. A computer-readable form of the sequence listing is also being submitted herewith. The content of the initial paper and computer-readable copies of the sequence listing are the same and include no new matter, as required by 37 C.F.R. §§ 1.825(a) and (b).

Objections to the Specification

The Examiner has objected to the specification because the “application does not contain an abstract of the disclosure as required by 37 C.F.R. §1.72(b).”

Applicants submit herewith an abstract of the invention on a separate sheet and, accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this objection to the specification.

The Examiner has also objected to the specification because “there are four nucleotide sequences with more [than] ten nucleotides in Figure 6. [The] Brief Description of the Drawings in the specification does not describe these nucleotide sequences and these nucleotide sequences do not have SEQ ID NOs.”

As indicated above, Applicants have amended the specification to add sequence identifiers in the Brief Description of the Drawings at page 19, lines 20-26 of the specification and in the sequences depicted in Figure 6. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection to the specification.

Claim Objections

The Examiner has objected to claims 4 and 10 because “‘an XbaI’ should be ‘a XbaI’; and (2) ‘XbaI’ should be ‘XbaI’”.

Applicants have amended claims 4 and 10 according to the Examiner’s recommendations. Accordingly, reconsideration and withdrawal of this objection to claims 4 and 10 is respectfully requested.

The Examiner has objected to claim 9 because, according to the Examiner, the recitation of “‘claims 1 to 4’ should be ‘any one of claims 1 to 4’”. The Examiner refers to claim 9 in this rejection, however, since claim 9 does not recite the phrase “claims 1 to 4,” Applicants assume that the Examiner intended to refer to claim 6. As such, Applicants have amended claim 6 to recite “any one of claims 1 to 4” and, accordingly, respectfully request reconsideration and withdrawal of this objection to claim 9.

The Examiner has objected to claim 9 because “‘io’ in step a) should be deleted”. Applicants have corrected this typographical error and, accordingly, respectfully request reconsideration and withdrawal of this objection to claim 9.

The Examiner has objected to claim 15 because “‘in to’ in line 2 should be ‘into’”. Applicants have corrected this typographical error and, accordingly, respectfully request reconsideration and withdrawal of this objection to claim 15.

Finally, the Examiner has objected to claim 17 because “‘polyketide synthesising enzyme domain DNA sequences’ should be ‘DNA sequences of polyketide synthesizing enzyme domain’”. Applicants have amended claim 17 consistent with the Examiner’s suggestions to recite “DNA sequences of polyketide synthesizing enzyme domain.” Accordingly, reconsideration and withdrawal of this objection to claim 17 is respectfully requested.

Rejections of Claims 1-17 and 21 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 1-17 and 21 under 35 U.S.C. §112, second paragraph “as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.”

With respect to claim 1, the Examiner is of the opinion that

in view of step a) of the claim it is unclear what is [the] relationship between the restriction site on the 3’ end of each DNA unit and a recognition site for a DNA modification enzyme. Does the restriction site on the 3’ end of each DNA unit and a recognition site for a DNA modification enzyme share some nucleotide sequences?

Without acquiescing to the validity of the Examiner’s rejection and in the interest of expediting prosecution and allowance of the pending claims, Applicants have amended step a) of claim 1, to specify that the 3’ *recognition sequence also comprises a DNA modification enzyme recognition sequence*.

Moreover, Applicants respectfully submit that, based on the plain language of the claims, the teachings in the specification, and the general knowledge in the art, one of skill in the art would have understood that the restriction enzyme recognition sequence at the 3’ end and the DNA modification enzyme recognition sequence may share one or more nucleotide residues such that the restriction enzyme recognition sequence will be recognized by the DNA modification enzyme (which is sequence specific) and rendered inaccessible to the restriction enzyme.

For example, Applicants’ specification teaches at page 7, lines 29, through page 8, lines 1-3, that when more than one of an accessible restriction site is present, a DNA modification enzyme may be employed so that the more than one accessible restriction site is not cleaved by

the restriction enzyme. Specifically, the specification teaches at, for example, page 19, lines 5-9 and lines 20-26, as well as Figure 6, that a restriction enzyme recognition sequence, such as TCTAGA (*i.e.*, a *Xba*I enzyme recognition sequence) shares one or more nucleotide residues with the DNA modification enzyme recognition sequence GATCTAGA (*i.e.*, a *dam* methylase) and that the replication of a vector comprising this restriction enzyme recognition sequence in an appropriate bacterial strain renders this sequence inaccessible to the restriction enzyme. Applicants' specification also teaches that a *Fok*I restriction enzyme recognition sequence (5'GGATG(N)₉3') may be made sensitive to a DNA modification enzyme, such as *dcm* methylase (whose recognition sequence is CCA/TGG) by the addition of the nucleotide residues CCA or CCT to the 5' end of the *Fok*I restriction enzyme recognition sequence (see page 25, lines 9-16 of the specification).

Furthermore, as evidenced by, for example, Roberts, R.J., *et al.* (2005) *Nucleic Acids Research* 33: D230-D232 (submitted herewith as Appendix A) and the publicly available database, REBASE (<http://rebase.neb.com/rebase/rebase.html>), it was well known in the art at the time of the invention that DNA modification enzymes and restriction enzymes may share one or more nucleotide residues.

In view of the foregoing, it is evident that claim 1 is clear and definite. Accordingly, the foregoing rejection has been rendered moot and Applicants respectfully request that this rejection of claim 1 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

The Examiner has also asserted that

[c]laim 1 recites the limitation 'the desired DNA unit' in step c) of the claim. There is insufficient antecedent basis for this limitation in the claim because steps a) and b) only have DNA unit and no desired DNA unit.

The Examiner is also of the opinion that

[c]laim 1 recites the limitation 'the ligated product' in step c) of the claim. There is insufficient antecedent basis for this limitation in the claim because steps a) and b) have no ligated product.

In addition, the Examiner is of the opinion that

[c]laim 1 recites the limitation 'the inserted DNA unit' in step c) of the claim. There is insufficient antecedent basis for this limitation in the claim because steps a) and b) have no inserted DNA unit.

Applicants respectfully submit that, in view of the amendments to claim 1, the foregoing rejections have been rendered moot. Accordingly, Applicants respectfully request that the foregoing rejections of claim 1 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 3, the Examiner is of the opinion that

[c]laim 3 recites the limitation 'dam methylase' in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no dam methylase in claims 1 and 2.

Applicants respectfully submit that, in view of the amendment to claim 3, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claim 3 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 4, the Examiner alleges that

[c]laim 4 recites the limitation 'the desired DNA unit' in step c) of the claim. There is insufficient antecedent basis for this limitation in the claim because steps a) and b) only have DNA unit and have no desired DNA unit.

The Examiner also asserts that

[c]laim 4 is rejected as vague and indefinite in view of step d) of the claim because it is unclear how to recovering a resulting plasmid since step b) does not limit a starting DNA construct as a plasmid.

Applicants respectfully submit that, in view of the amendments to claim 4, the foregoing rejections have been rendered moot. Accordingly, Applicants respectfully request that the rejection of claim 4 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 6, the Examiner is of the opinion that

[c]laim 6 recites the limitation 'the fragment' in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no word 'fragment' in claims 1-4.

Applicants respectfully submit that, in view of the amendments to claim 6, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claim 6 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 8, the Examiner alleges that "it is unclear how to replicate the ligated product in a dam- strain of *E. coli* by means of a suitable vector."

Applicants respectfully submit that, in view of the amendments to claim 8, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claim 8 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claims 9 and 10, the Examiner is of the opinion that "[i]t is unclear that a 'desired other DNA unit' in step c) or 'a desired DNA unit' in step d) are identical to one of the other DNA units in step b) or not."

Applicants respectfully submit that, in view of the amendments to claims 9 and 10, the foregoing rejection has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claims 9 and 10 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 13, the Examiner is of the opinion that "[c]laim 13 is vague and indefinite because it is unclear the solid phase is split and mixed with what."

Without acquiescing to the validity of the Examiner's rejection and in the interest of expediting prosecution and allowance of the pending claims, Applicants have amended claim 13 to recite that *the solid phase is combined with a subsequent desired DNA unit in step c)* to

make several different assemblies. Accordingly, the foregoing rejection has been rendered moot and Applicants respectfully request that this rejection of claim 13 under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

With respect to claim 15, the Examiner states that “[i]t is unclear what means ‘a host capable of expressing the protein encoded by the vector’”.

In the interest of expediting prosecution and allowance of the pending claims, and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended claim 15, thereby obviating this rejection. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

SUMMARY

In view of the above amendments, Applicants believe that the present application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Applicants believe that no fee is due with this communication. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. SHW-009US from which the undersigned is authorized to draw.

Dated: April 3, 2006

Respectfully submitted,

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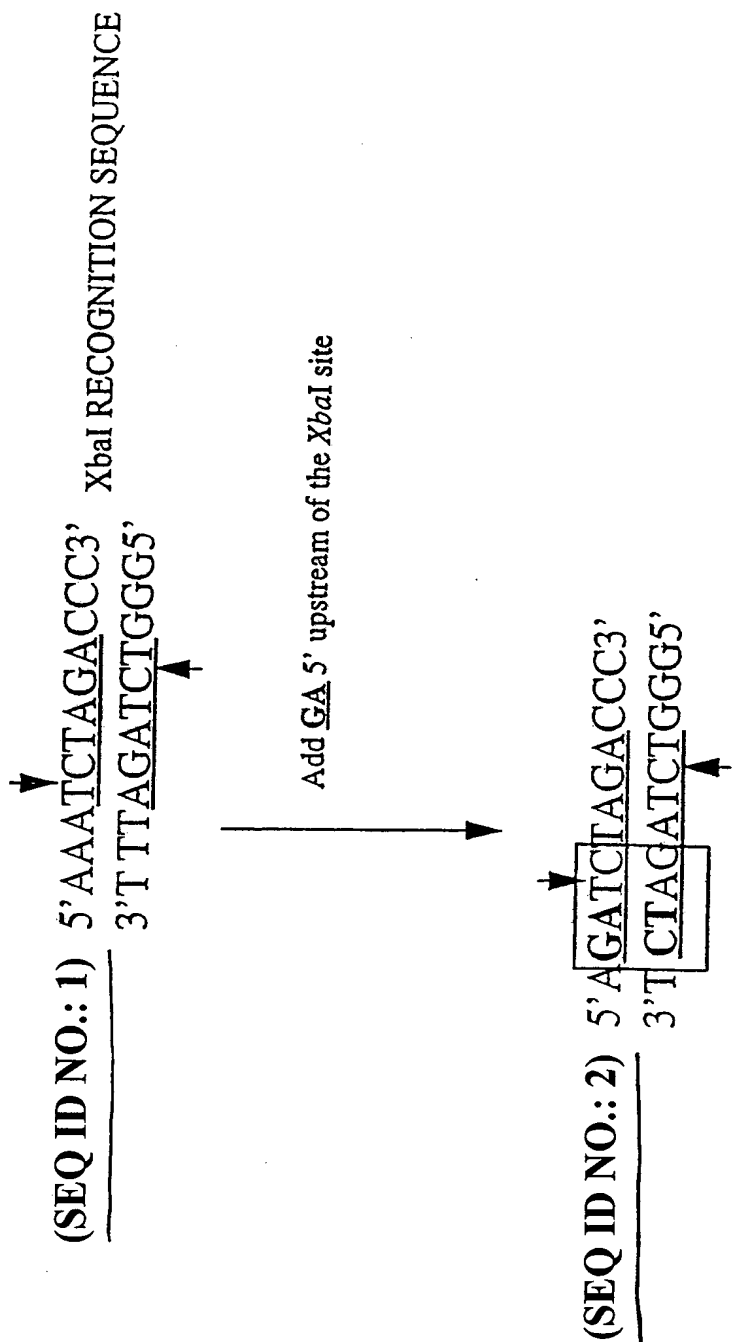


FIG.6.



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S.I. 1 ATGGCAGGAACCGACCGCGAGAAGGCCCTGGACGCCGCGCTCGCACAGAT 50
S.a. 1 ATGGCAGGAACCGACCGCGAGAAGGCTCTTGACGCCGCACTCGCACAGAT 50
51 TGAACGGCAATTTCGGCAAGGGCGCGGTTCATGCGCATGGGTGACCGGACCA 100
51 TGAACGGCAGTTTCGGCAAGGGCGCGGTTCATGCGCATGGGCGACCGGTCTGA 100
101 ACGAGCCCATCGAGGTTCATCCCGACCGGGTCTACCGCGCTCGACGTGGCC 150
101 AGGAGCCCATCGAGGTTCATCCCGACCGGGTTCGACCGCGCTCGACGTGGCC 150
151 CTCGGCGTCGGAGGCATCCCGCGTGGCCGTGTCGTGGAGGTCTACGGCCC 200
151 CTCGGCGTCGGCGGCGCTGCCGCGCGCCGCGTCATCGAGGTCTACGGTCC 200
201 CGAGTCCTCGGGCAAGACGACCCTGACCCTGCACGCGGTGGCGAACGCGC 250
201 GGAGTCCTCCGGTAAGACGACCCTGACCCTGCACGCGGTGGCGAACGCGC 250
251 AGAAGGCCGGCGGCCAGGTTCGCGTTTCGTGGACGCCGAGCACGCCCTCGAC 300
251 AGAAGGCCGGCGGCCAGGTGGCGTTTCGTGGACGCCGAGCACGCCCTCGAC 300
301 CCCGAGTACGCGAAGAAGCTCGGTGTCGACATCGACAACCTGATCCTGTC 350
301 CCCGAGTACGCCCAGAAGCTCGGCGTCGACATCGACAACCTGATCCTGTC 350
351 CCAGCCGGACAACGGTGAGCAGGCCCTGGAGATCGTGGACATGCTGGTCC 400
351 CCAGCCGGACAACGGTGAGCAGGCCCTGGAGATCGTGGACATGCTGGTCC 400
401 GCTCCGGCGCCCTCGACCTCATCGTCATCGACTCCGTCGCCGCGCTCGTC 450
401 GCTCCGGCGCCCTCGACCTCATCGTCATCGACTCCGTCGCCGCGCTCGTC 450
451 CCGCGCGCGGAGATCGAGGGCGAGATGGGCGACAGCCACGTCGGTCTGCA 500
451 CCGCGCGCGGAGATCGAGGGCGAGATGGGTGACAGCCACGTCGGTCTCCA 500
501 GGCCCGGCTGATGAGCCAGGCCCTGCGGAAGATCACCAGCGCGCTCAACC 550 (SEQ ID NO.: 5)
501 GGCCCGGCTGATGAGCCAGGCGCTCCGGAAGATCACCAGCGCGCTCAACC 550 (SEQ ID NO.: 6)

FIG.14.A.



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S.l. 551 AGTCCAAGACCACCGCGATCTTCATCAACCAGCTCCGCGAGAAGATCGGC 600
|||||
S.a. 551 AGTCCAAGACCACCGCGATCTTCATCAACCAGCTCCGCGAGAAGATCGGC 600
601 GTGATGTTCTGGCTCCCCGAGACCACGACCGGTGGCCGGGCACTGAAGTT 650
||
601 GTCATGTTCTGGCTCCCCGAGACCACGACCGGTGGCCGGGCGCTCAAGTT 650
651 CTACGCCTCGGTGCGACTCGACATCCGGCGTATCGAGACGCTGAAGGACG 700
|||||
651 CTACGCCTCGGTGCGACTCGACATCCGACGCATCGAGACGCTCAAGGACG 700
701 GCACCGACGCGGTCTGGCAACCGCACCCGCGTCAAGGTGGTCAAGAACAAG 750
|||||
701 GCACCGACGCGGTCTGGCAACCGCACGCGCGTCAAGGTCTGTCAGAACAAG 750
751 GTCGCGCCGCCCTTCAAGCAGGCCGAGTTCGACATCCTCTACGGCCAGGG 800
|||||
751 GTCGCGCCGCCCTTCAAGCAGGCCGAGTTCGACATCCTCTACGGCCAGGG 800
801 CATCAGCCGCGAGGGCGGTCTGATCGACATGGGCGTGGAGAACGGCTTCG 850
|||||
801 CATCAGCCGCGAGGGCGGTCTGATCGACATGGGCGTGGAGCACGGCTTCG 850
851 TCCGCAAGGCCGCGCCTGGTACACGTACGAGGGCGACCAGCTCGGTTCAG 900
|||||
851 TCCGCAAGGCCGCGCCTGGTACACGTACGAGGGCGACCAGCTCGGCCAG 900
901 GGCAAGGAGAACGCGCGCAACTTCCTGAAGGACAACCCCGACCTGGCCAA 950
|||||
901 GGCAAGGAGAACGCGCGCAACTTCCTGAAGGACAACCCCGACCTCGCCAA 950
951 CGAGATCGAGAAGAAGATCAAGCAGAAGCTGGGCGTGGCGTGACCCCG 1000
|||||
951 CGAGATCGAGAAGAAGATCAAGGAGAAGCTGGGCGTGGGAGTCCGTCCCG 1000
1001 AGGA...GTCGGCCACCGAGCCCCGGCGCGGACGCGCCTCCGCGGCCCG 1047
|||||
1001 AGGAGCCGACGGCCACCGAGTCCGGACCGGA.....CGCCGCGACG 1041
1048 GCCGACGCCGACCGGCGGTGCCCGCACCCACGACCGCCAAGGCCACCAA 1097
|||||
1042 GCCGAATCCGACCGGCGGTGCCCGCGCCCGGACCGCCAAGGTCACCAA 1091
1098 GTCCAAGGCCGCGGCGAGCCAAGAGCTGA 1125 (SEQ ID NO.: 5)
|||||
1092 GGCCAAGGCCGCGGCGAGCCAAGAGCTGA 1119 (SEQ ID NO.: 6)

FIG.14.B.